

WE CLAIM:

1. A non-human mammalian animal comprising a non-naturally occurring mutation in a sensin gene.
2. A non-human mammalian animal according to claim 1, wherein the resulting mutated sensin gene causes a deficit in a motor-related phenotype in said mammalian animal.
3. A non-human mammalian animal according to claim 1, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 1.
4. A non-human mammalian animal according to claim 1, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 2.
5. A non-human mammalian animal according to claim 1, wherein said mutated sensin gene comprises a mutation in a splice site.
6. A non-human mammalian animal according to claim 5, wherein said mutation in a splice site is a single nucleotide change in a splice donor site.
7. A non-human mammalian animal according to claim 6, wherein said splice donor site is GA.
8. A non-human mammalian animal according to claim 6, wherein said mutation in a splice site results in deletion of an exon from a cDNA expressed from said gene.
9. A non-human mammalian animal according to claim 8, wherein said cDNA is expressed as a protein comprising a deletion of the sequence KEDLKWSSLLQVIE (SEQ ID NO: 3) or KVDLKWNSLLKIIE (SEQ ID NO: 4).
10. A non-human mammalian animal according to claim 1, wherein said one or more mammals are mice expressing a cDNA encoding the protein of SEQ ID NO: 5.
11. A non-human mammalian animal according to claim 1, wherein said mammalian animal is a mouse expressing a cDNA encoding the protein of SEQ ID NO: 6.

12. A non-human mammalian animal according to claim 1, wherein said mouse is homozygous for said non-naturally occurring mutation in a sensin gene.

13. A colony comprising a plurality of non-human mammalian animals comprising an identical non-naturally occurring mutation in a sensin gene.

14. A method for screening for modulators of motor activity in a mammal, comprising:

contacting one or more mammals with one or more test compounds, and

determining whether said test compound(s) alter(s) a sensin-mediated motor-related phenotype, thereby identifying said modulator(s).

15. A method according to claim 14, wherein said one or more mammals comprise a mutation in a sensin gene, wherein the resulting mutated sensin gene causes a deficit in a motor-related phenotype in said one or more mammals.

16. A method according to claim 14, wherein said one or more test compounds are nucleic acids.

17. A method according to claim 16, wherein said nucleic acids are antisense molecules.

18. A method according to claim 16, wherein said nucleic acids are RNAi molecules.

19. A method according to claim 15, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 1.

20. A method according to claim 15, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 2.

21. A method according to claim 15, wherein said mutated sensin gene comprises a mutation in a splice site.

22. A method according to claim 21, wherein said mutation in a splice site is a single nucleotide change in a splice donor site.

23. A method according to claim 22, wherein said splice donor site is GA.

24. A method according to claim 22, wherein said mutation in a splice site results in deletion of an exon from a cDNA expressed from said gene.

25. A method according to claim 24, wherein said cDNA is expressed as a protein comprising a deletion of the sequence KEDLKWSSLLQVIE (SEQ ID NO: 3) or KVDLKWNSLLKIIE (SEQ ID NO: 4).

26. A method according to claim 15, wherein said one or more mammals are mice expressing a cDNA encoding the protein of SEQ ID NO: 5.

27. A method according to claim 15, wherein said one or more mammals are mice expressing a cDNA encoding the protein of SEQ ID NO: 6.

28. A method for screening for modulators of motor activity in a mammal, comprising:

contacting one or more mammals with one or more test compounds, and

determining whether said test compound(s) alter(s) expression of a mutated sensin gene, or alter(s) expression of a wild type sensin gene, thereby identifying said modulator(s).

29. A method according to claim 28, wherein said one or more test compounds are nucleic acids.

30. A method according to claim 29, wherein said nucleic acids are antisense molecules.

31. A method according to claim 29, wherein said nucleic acids are RNAi molecules.

32. A method according to claim 28, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 1.

33. A method according to claim 28, wherein said mutated sensin gene is expressed as a cDNA having substantial sequence homology with SEQ ID NO: 2.

34. A method according to claim 28, wherein said mutated sensin gene comprises a mutation in a splice site.

35. A method according to claim 34, wherein said mutation in a splice site is a single nucleotide change in a splice donor site.

36. A method according to claim 35, wherein said splice donor site is GA.

37. A method according to claim 35, wherein said mutation in a splice site results in deletion of an exon from a cDNA expressed from said gene.

38. A method according to claim 37, wherein said cDNA is expressed as a protein comprising a deletion of the sequence KEDLKWSSLLQVIE (SEQ ID NO: 3) or KVDLKWNSLLKIIE (SEQ ID NO: 4).

39. A method according to claim 28, wherein said one or more mammals are mice expressing a cDNA encoding the protein of SEQ ID NO: 5.

40. A method according to claim 28, wherein said one or more mammals are mice expressing a cDNA encoding the protein of SEQ ID NO: 6.

41. A method comprising:

contacting a subject in need thereof with one or more compounds in an amount sufficient to alter a motor activity in said subject, wherein said modulators of motor activity alter a sensin-mediated motor-related phenotype in a mammalian animal.

42. A method according to claim 41, wherein said subject comprises a mutation in a sensin gene.

43. A method according to claim 41, wherein said mammalian animal is a mouse expressing the protein of SEQ ID NO: 5.

44. A method according to claim 41, wherein said non-human mammalian animal is a mouse expressing the protein of SEQ ID NO: 6.

45. A method for determining the level of a sensin polypeptide in a sample, comprising:

assaying for said sensin polypeptide with an antibody, or fragment thereof, that specifically binds to said sensin polypeptide.

46. A method according to claim 45, wherein said antibody binds to the protein of SEQ ID NO: 5.

47. A method according to claim 45, wherein said antibody binds to the protein of SEQ ID NO: 6.

48. A method according to claim 45, wherein said antibody comprises an affinity for a mutated sensin polypeptide greater than an affinity for a wild type sensin polypeptide.

49. A method for diagnosing a motor deficit in a subject, comprising:

determining whether said subject comprises a mutation in a sensin nucleic acid sequence.

50. A method according to claim 49, wherein said nucleic acid sequence is selected from the group consisting of a genomic DNA sequence and an expressed RNA sequence.

51. A method for identifying a subject suitable for treatment with an one or more compounds having an effect on a motor deficit, comprising:

determining whether said subject comprises a mutation in a sensin nucleic acid sequence, wherein the presence of said mutation identifies said subject for inclusion or exclusion from said treatment.

52. A kit for determining whether a sample comprises a mutation in a sensin nucleic acid sequence, comprising:

an assay component that detects a mutation in a sensin nucleic acid sequence; and
instructions for performing said determination.

53. An isolated sensin polypeptide.

54. An isolated polypeptide comprising at least 15 consecutive amino acid residues of:

SEQ ID NO: 5;

SEQ ID NO: 6;

SEQ ID NO: 7;

SEQ ID NO: 8;

SEQ ID NO: 9;

SEQ ID NO: 10; or

SEQ ID NO: 11.

55. An isolated polypeptide comprising the sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

56. An isolated sensin nucleic acid.

57. An isolated nucleic acid molecule encoding a polypeptide comprising at least 15 consecutive amino acid residues of :

SEQ ID NO: 5;

SEQ ID NO: 6;

SEQ ID NO: 7;

SEQ ID NO: 8;

SEQ ID NO: 9;

SEQ ID NO: 10; or

SEQ ID NO: 11.

58. An isolated nucleic acid molecule encoding the sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

59. A recombinant vector comprising a nucleic acid sequence encoding a polypeptide comprising at least 15 consecutive amino acid residues of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, or SEQ ID NO: 11; or a nucleic acid sequence encoding a polypeptide having the sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

60. A recombinant vector according to claim 59, wherein said vector is an expression vector adapted for expression of a eukaryotic coding sequence.

61. A recombinant cell comprising the recombinant vector of claim 59.

62. An antibody that specifically binds to a sensin polypeptide.

63. A method of identifying one or more genes related to mammalian motor function, comprising:

introducing one or more mutations into the genome of a mouse comprising a nucleic acid encoding a mutated sensin gene, wherein the mutated sensin gene causes a deficit in a motor-related phenotype in said mouse; and

identifying mutations that affect said sensin-mediated motor-related phenotype of said mouse.

64. A method comprising:

expressing in one or more cells of a subject in need thereof an sensin polypeptide encoded by an expression construct in which an sensin nucleic acid is operably inserted downstream in the direction of transcription of a transcriptional regulatory region functional in said one or more cells.

65. A method according to claim 64, wherein a deficit in a motor-related phenotype is altered in said subject following said expressing step.

66. A method according to claim 64, wherein said expression construct is introduced into one or more cells ex vivo, and said cells are subsequently administered to said subject.

67. A method of making a non-human mammalian animal, comprising:

introducing one or more mutations into a sensin gene of said non-human mammalian animal.
68. A method of identifying one or more genes related to motor function, comprising:

determining whether said genes encode polypeptides that bind to an isolated sensin polypeptide.